

REMARKS

Claim 5, 30 and 54-56 have been canceled.

Claims 1-3, 10-11, 25-27, 29 and 51 have been amended.

Claims 58-63 have been added.

Claim 1, as amended, is directed to a method of characterizing a metabolic phenotype of an individual, comprising administering to said individual a probe substrate specific to a metabolic pathway; detecting metabolites of said probe substrate in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and characterizing said metabolic phenotype of said individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Support for the amendment to Claim 1 is found, for example, in the specification at page 57, line 29 to page 58, line 10 and page 59, line 6 to line 15.

Claim 2, as amended, is directed to the method of claim 1 which further comprises a step i) after step b): i) quantifying a ratio of respective detected metabolites for said probe substrate in said biological sample. Support for the amendment to Claim 2 is found, for example, in the specification at page 57, line 29 to page 58, line 10 and page 61, line 24 to page 62, line 6.

Claim 3, as amended, is directed to the method of claim 2, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio and peak height ratio. Support for the amendment to Claim 3 is found, for example, in the specification at page 57, line 29 to page 58, line 10; page 61, line 24 to page 62, line 6; and originally-filed Claim 3.

Claims 10 and 11 have been amended to correct obvious typographical errors. Support for "aptamer" is found in the specification, for example, on page 113, line 18 and support for "molecularly imprinted" polymers is found in the specification, for example, on page 116, lines 7-10. Claim 25, as amended, is directed to the method of Claim 1, wherein step b is effected using a quantitative detection instrument. Support for this amendment is found in the specification, for example, on page 212, lines 10-14.

Claim 26, as amended, is directed to the method according to claim 1, step c) wherein said metabolic phenotype is based on enzyme-specific determinant. Support for the amendment to Claim 26 is found, for example, in the specification in Table 1 and originally-filed Claim 26.

Claim 27, as amended, is directed to the method according to claim 26 wherein said metabolic phenotype is comprised of at least one metabolite indicative of an individual's metabolic capacity for at least one drug metabolizing enzyme. Support for the amendment to Claim 27 is found, for example, in the specification at page 57, line 26 to page 58, line 10.

Claim 29, as amended, is directed to the method of claim 2, wherein step a) is effected using at least two probe substrates and wherein each probe substrate is specific to at least one metabolic pathway of interest. Support for the amendment to Claim 29 is found, for example, at page 58, lines 1-24 and originally filed Claim 29.

Claim 51, as amended, is directed to a method of using a metabolic phenotype of claim 1 for determining a combination drug therapy wherein an individual's phenotype is indicative of a fast metabolizer, and a corresponding inhibitor of a drug is selected for combined treatment with the drug to improve the therapeutic effect of the drug in said individual. Support for the amendment to Claim 51 is found, for example, in the specification in Table 3 and in the originally-filed Claim 51.

New Claim 58 is directed to a method of characterizing a metabolic phenotype of an individual. Support for new Claim 58 is found, for example, in the specification at page 57, line 29 to page 58, line 10.

New Claim 59 is directed to a method of determining an individual's drug metabolizing ability. Support for new Claim 59 is found, for example, in the specification at page 57, line 29 to page 58, line 15.

New Claims 60 and 61 are directed to the methods of claims 59 and 60, respectively wherein the individual is a mammal and wherein the mammal is a human. Support for new Claims 60 and 61 is found, for example, throughout the specification and claims, in originally-filed Claims 60 and 61.

New Claim 62 is directed to a method of individualizing a selected safe and therapeutically effective drug treatment dosing regimen for an individual. Support for new Claim 62 is found, for example, in the specification 58, line 16 to page 59, line 26.

New Claim 63 is directed to a method of characterizing a metabolic phenotype of an individual. Support for new Claim 63 is found, for example, in the specification at page 57, line 29 to page 58, line 10.

No new matter has been added by the amendments. Therefore, entry of the amendments into the application is respectfully requested.

Rejection of Claims 1-30, 51 and 54-56 Under 35 U.S.C. § 112, first paragraph

The Examiner has rejected Claims 1-30, 51 and 54-56 under 35 U.S.C. § 112, first paragraph. The Examiner states that:

Applicant is advised that the “biological sample”, according to the definition presented on page 62, lines 20-25 of the instant specification, includes “breath” samples. However, there appears to be no disclosure presented in the instant specification, which would provide support for detecting metabolites in breath samples. Applicant disclose[s] a list of assay and sensors... but none of the sensor[s] is known to detect a *volatile [breath]* sample. (See page 125-132) It would be undue experimentation for one skilled in the art to discover how to characterize a multi-determinant metabolic phenotype using a breath sample for analysis.

As discussed above, Claims 1-3, 10-11, 25-27, 29 and 51 have been amended. Claims 5, 30 and 54-56 have been canceled. As amended, Claim 1 recites “a method of characterizing a metabolic phenotype of an individual, comprising administering to said individual a probe substrate specific to a metabolic pathway; detecting metabolites of said probe substrate in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and characterizing said metabolic phenotype of said individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual.” As amended, Claim 1 does not recite a “breath sample.” Claims 2-4, 6-29 and 51, which depend from Claim 1, also do not encompass breath samples.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection to Claims 1-30, 51 and 54-56 Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1-30, 51 and 54-56 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Metabolic Characteristics

The Examiner states that, with respect to Claim 1, line 3, the term “metabolic characteristics” is vague and indefinite. The Examiner further states that the meaning of the term “metabolic characteristics” is unclear.

As discussed above, Claims 1-3, 10-11, 25-27, 29 and 51 have been amended. Claims 5, 30 and 54-56 have been canceled. As amended, Claim 1 recites “a method of characterizing a metabolic phenotype of an individual, comprising administering to said individual a probe substrate specific to a metabolic pathway; detecting metabolites of said probe substrate in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and characterizing said metabolic phenotype of said individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual.” As amended, Claim 1 does not recite “metabolic characteristics.” Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Under the curve

The Examiner states that “[w]ith respect to claim 3, line 2, ‘under the curve’ lacks antecedent basis.”

As discussed above, Claim 3 has been amended. As amended, Claim 3 recites “the method of claim 2, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio and peak height ratio.” As amended, Claim 3 does not recite “ratio of area under the curve.” Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Ratio of Area Under the Curve

The Examiner states that “[w]ith respect to claim 3, ratio of area under the curve’ is vague and indefinite. The Examiner further states that “[i]t is unclear what is the area under the curve.”

As discussed above, Claim 3 has been amended. As amended, Claim 3 recites “the method of claim 2, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio and peak height ratio.” As amended, Claim 3 does not recite “ratio of

area under the curve.” Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Signal Peak Height Ratio

The Examiner states that “[w]ith respect to claim 3, ‘signal peak height ratio’ is vague and indefinite.” The Examiner further states that “[i]t is unclear what is the ‘signal peak height ratio’ in the context.”

Applicants respectfully disagree. Applicants disclose immunosensors, such as indirect sensors which use signal-generating labels to detect, for example, NAT2 phenotype using caffeine as a probe substrate. See, for example, the specification at page 118, line 13, to page 119, line 21. Applicants further disclose measuring the peak height ratio of the signals. See, for example, page 154, line 7 to page 159, line 8. Therefore, the term “signal peak height ratio” is not indefinite. To further clarify the term, Claim 3 has been amended to delete the word “signal.” Reconsideration and withdrawal of the rejection is respectfully requested.

Molecular Imprinted Polymer

The Examiner states that “[w]ith respect to claim 10, ‘molecular imprinted polymer’ is vague and indefinite. The Examiner further states that “[i]t is unclear what is the molecular imprinted polymer.”

As discussed above, Claim 10 has been amended to correct an obvious typographical error. As amended, Claim 10 recites “the method of claim 6, wherein said affinity complexation agent is a molecularly imprinted polymer.” Molecularly imprinted polymers are well known in the art and are described in the specification. See, for example, the specification at page 115, line 18 to page 116, line 15. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection to Claims 1-6, 26-30, 51 and 54-56 under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1-6, 26-30, 51 and 54-56 under 35 U.S.C. § 102(b) as being anticipated by Desta *et al.* (“Effect of Clarithromycin on the Pharmacokinetics and Pharmacodynamics of Pimozide in Healthy Poor and Extensive Metabolizers of Cytochrome P450 2D6 (CYP2D6),” *Clin. Pharmacol. Ther.*, 65:10-20 (1999)). The Examiner states that:

Desta *et al.* teach a method of evaluating the effect of antibiotics clarithromycin on the metabolism of pimozide on individuals [suffering from] Gilles de la Tourette’s. (See abstract) Desta *et al.* use pharmacokinetic analysis, including concentration-time curve, terminal half-life, clearance and volume distribution, peak and ratio, to measure the metabolites in the plasma from the individuals dosed with pimozide, antibiotics or both. (See Methods; Data Analysis; Figures 1-3) The metabolic enzymes [involved] in the [metabolism] are CYP2D6 and CYP3A. (See abstract; Introduction) The magnitudes and variations of metabolites reflect the multi-determinant metabolic phenotype with respect to the therapeutic agents. (See Table I-III) The goal of the study is to have clinical application, e.g., with considerations of the metabolic profile of the therapeutics, to optimize the chemical treatments on the Tourette’s patients. (page 19, second paragraph) It is also inherently precautionary measures in clinical practice, including drug resistance, susceptibility, and renal function when patients are to be treated with antibiotics.

Applicant respectfully disagrees. As discussed above, Claims 1-3, 25-27 and 29 and 51 have been amended. Claims 5, 30 and 54-56 have been canceled.

Desta *et al.* does not expressly or inherently teach the claimed invention. Applicant’s Claim 1, as amended, recites “a method of characterizing a metabolic phenotype of an individual, comprising administering to said individual a probe substrate specific to a metabolic pathway; detecting metabolites of said probe substrate in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and characterizing said metabolic phenotype of said individual based on detected metabolites *to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual.*” (emphasis added) The remaining pending claims subject to this rejection are dependent upon Claim 1 and contain the same limitation.

Desta *et al.* describe a clinical study evaluating the use of clarithromycin, a substrate and inhibitor of CYP3A, in conjunction with pimozide, a substrate for CYP3A, and the effect on

cardiological adverse events. Further, Desta *et al.* note that clarithromycin inhibited CYP3A-mediated pimozone metabolism and the resulting elevation in plasma concentration may increase the risk of pimozone cardiotoxicity.

Desta *et al.* do not expressly anticipate the claimed invention. Generally, all of the elements of the claimed invention must be found within a single reference in order to anticipate, either expressly or inherently, under 35 U.S.C. §102. As stated in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986), for example, "[i]t is axiomatic that for prior art to anticipate under §102 it has to meet every element of the claimed invention, and that such a determination is one of fact."

Desta *et al.* do not teach a method of characterizing the metabolic phenotype of the individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen. Although Desta *et al.* measured metabolism of a second pathway, CYP2D6, they did not correlate or connect rate of metabolism with individualized treatment.

Further, Desta *et al.* do not inherently teach the claimed invention. The Manual of Patent Examining Procedure (MPEP 8th edition, May 2004 revision, § 2112) articulates the requirements of a rejection based on inherency. Specifically, under the subheading "Examiner Must Provide Rationale for Evidence Tending to Show Inherency," the MPEP quotes a decision by the Board of Patent Appeals and Interferences in *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original), which states:

In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art.

As explained by the MPEP, the Examiner in *Ex parte Levy* argued, without providing support, that a reference inherently included a limitation of the Appellants' invention. According to the MPEP, the Board of Patent Appeals and Interferences reversed the Examiner's decision because the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency. See MPEP at page 2100-52.

Further, the doctrine of inherency is based on the necessary presence of an element described in a reference; it is not sufficient to establish that a presence of the element is a

probability or a possibility. For example, as is also stated in the MPEP at § 2112 (emphasis in original): The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. (Citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993).)

The Examiner presented no evidence that Desta *et al.* would necessarily characterize a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. In fact, the authors noted no significant changes in pimozone pharmacokinetics in poor metabolizers relative to extensive metabolizers. (See page 18, bottom of column 2). They also noted that, although the activity of CYP3A has been reported to be higher in women than in men, no significant effect of gender on the pharmacokinetic or pharmacodynamic parameters tested was found. *Id.*

Desta *et al.* does not expressly or inherently teach characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Thus, the rejected claims are novel. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection to Claims 1-10, 14-15, 18, 25-30, 51 and 54-56 under 35 U.S.C. § 102(a)

The Examiner has rejected Claims 1-10, 14-15, 18, 25-30, 51 and 54-56 under 35 U.S.C. § 102(a) as being anticipated by Wainer *et al.* ("A Competitive Enzyme Linked Immunosorbent Assay for the Determination of *N*-acetyltransferase (NAT2) Phenotypes," *J. Pharm. Biomed. Anal.*, 13(9): 1079-1086 (1995). The Examiner states that:

Wainer *et al.* teach using probe drugs, such as caffeine to study phenotypic characteristics of NAT2 (N-acetyltransferase-2) in individuals. (See abstract) Wainer *et al.* teach that administering the probe drugs to [an] individual and analyze the plurality of metabolites from urine samples, i.e. AAMU to 1-methylxanthine (1X), corresponding to the metabolic profile of the individuals in response to the probe drug. (See Table 2) Wainer *et al.* teach a rapid and convenient ELISA assay instead of conventional HPLC. (See Method and Materials) The assay involves using polyclonal antibodies against the phenotypic determinants in response to the probe drugs. (See Materials and Method)

Applicant respectfully disagrees. As discussed above, Claims 1-3, 10, 25-27, 29 and 51 have been amended. Claims 5, 30 and 54-56 have been canceled.

Wainer *et al.* do not expressly or inherently disclose the claimed invention. Applicant's Claim 1, as amended, recites "a method of characterizing a metabolic phenotype of an individual, comprising administering to said individual a probe substrate specific to a metabolic pathway; detecting metabolites of said probe substrate in a biological sample from said individual in response to said probe substrate, wherein said biological sample is not a breath sample; and characterizing said metabolic phenotype of said individual based on detected metabolites to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual." The pending claims subject to this rejection are dependent upon Claim 1 and contain the same limitation.

Wainer *et al.* disclose a method of characterizing a metabolic phenotype of an individual. More specifically, Wainer *et al.* disclose the method of using caffeine as a substrate to study phenotypic characteristics of NAT2 (N-acetyltransferase-2) in individuals.

Wainer *et al.* do not expressly anticipate the claimed invention. As discussed above, generally, all of the elements of the claimed invention must be found within a single reference in order to anticipate, either expressly or inherently, under 35 U.S.C. §102. Nowhere do Wainer *et al.* disclose a method of characterizing the metabolic phenotype of the individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen.

Further, Wainer *et al.* do not inherently disclose the claimed invention. There is no indication in the reference that Wainer *et al.* would necessarily characterize a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual.

Wainer *et al.* do not expressly or inherently disclose characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Thus, the rejected claims are novel. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection to Claims 11-12 under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 11-12 under 35 U.S.C. 103(a) as being unpatentable over Wainer *et al.* in view of Cubicciotti *et al.* (U.S. 6,287,765). The Examiner states that:

Wainer *et al.* reference has been discussed but does not explicitly teach using aptamer or receptor for drug metabolites study. Cubicciotti *et al.* reveal that it is known in the art that aptamer or receptor would bind to the therapeutic metabolic target, and therefore can be detected by modified ELISA [to] increase sensitivity, cost-effectiveness and reproducibility. (See example 21 and example 22) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer *et al.* with the affinity complexation agent as taught by Cubicciotti *et al.* since it is known in the pharmaceutical practice to detect the binding of receptor or aptamer to the target compound to increase sensitivity, cost-effectiveness and reproducibility.

Claims 11 and 12 are dependent upon Claim 1, which has been amended. As discussed above, Claim 11 has been amended. Claim 11 and Claim 12 are not obvious over Wainer *et al.* in view of Cubicciotti *et al.* because, as established above, Wainer *et al.* does not teach or disclose a method of characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Therefore, the cited references do not reasonably suggest the claimed invention, because using an affinity complexation agent, such as an aptamer or receptor, as disclosed by Cubicciotti *et al.*, in the methods taught by Wainer *et al.*, would not result in the claimed invention. In view of the foregoing, reconsideration and withdrawal of the rejection is requested.

Rejection to Claim 13 under 35 U.S.C. § 103(a)

The Examiner has rejected Claim 13 under 35 U.S.C. 103(a) as being unpatentable over Wainer *et al.* in view of Beste *et al.* ("Small Antibody-like Proteins with Prescribed Ligand Specificities Derived From the Lipocalin Fold," *Pro. Natl. Acad. Sci.*, 96:1898-1903 (1999)). The Examiner states that:

Wainer reference has been discussed but does not explicitly teach using anticalin for binding assay. Beste *et al.* teach that using lipocalin as an alternative for conventional antibodies for ligand binding assay. (See abstract) Beste *et al.* reveal that conventional antibodies have certain disadvantages such as larger molecules

[which are] not easy to manipulate, or two polypeptide chains [which] complicate [the] cloning procedure. (page 1898, left column, first paragraph) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Desta and Wainer *et al.* with the alternative anticalin as taught by Beste *et al.* for convenience and economy in detecting the target molecules.

Claim 13 is dependent upon Claim 1, which has been amended. The invention of Claim 13 is not obvious over Wainer *et al.* in view of Beste *et al.* because, as established above, Wainer *et al.* do not teach or disclose a method of characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Therefore, the cited references do not reasonably suggest the claimed invention, because using an affinity complexation agent, such as an anticalin, as disclosed by Beste *et al.*, in the methods taught by Wainer *et al.*, would not result in the claimed invention. In view of the foregoing, reconsideration and withdrawal of the rejection is requested.

Rejection to Claims 16-17 under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 16-17 under 35 U.S.C. 103(a) as being unpatentable over Wainer *et al.* in view of Pronovost *et al.* (U.S. 5,786,220). The Examiner states that:

Desta and Wainer references have been discussed but do not explicitly teach using dipstick immunoassay to detect metabolites in a sample. Pronovost *et al.* teach using [dipstick] for quick detecting the presence of metabolites in [a] patient sample. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Desta and Wainer *et al.* with [the] dipstick immunoassay as taught by Pronovost *et al.* to detect metabolites in a patient sample in a time-saving manner.

Claims 16 and 17 are dependent upon Claim 1, which has been amended. Claims 16 and 17 not obvious over Wainer *et al.* in view of Pronovost *et al.* because, as established above, Wainer *et al.* do not teach or disclose a method of characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Therefore, the cited references do not reasonably suggest the claimed invention, because using a rapid immunoassay, based on Rapid Analyte Measurement Platform (RAMP) technology, as disclosed by Pronovost *et al.*, in the methods taught by Wainer

et al., would not result in the claimed invention. In view of the foregoing, reconsideration and withdrawal of the rejection is requested.

Rejection to Claims 18-23 under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 18-23 under 35 U.S.C. 103(a) as being unpatentable over Wainer *et al.* in view of Rabbany *et al.* ("Optical Immunosensors," *Crit. Rev. Biomed. Eng.*, 22:307-346 (1994)). The Examiner states that:

Wainer *et al.* reference has been discussed but does not explicitly teach using various biosensors for detection purposes. Rabbany *et al.* review the immunosensors in applications to the detection of analytes in samples, including optical piezoelectric, electrochemical sensors. (See page 320-340) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer *et al.* with alternative biosensors as taught by [Rabbany] *et al.* since it is known in the art to use the biosensor to detect target molecules in the sample.

Claims 18-23 are dependent upon Claim 1, which has been amended. Claims 18-23 are not obvious over Wainer *et al.* in view of Rabbany *et al.* because, as established above, Wainer *et al.* do not teach or disclose a method of characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Therefore, the cited references do not reasonably suggest the claimed invention, because using immunoassays and biosensors, as disclosed by Rabbany *et al.*, in the methods taught by Wainer *et al.*, would not result in the claimed invention. In view of the foregoing, reconsideration and withdrawal of the rejection is requested.

Rejection to Claim 24 under 35 U.S.C. § 103(a)

The Examiner has rejected Claim 24 under 35 U.S.C. 103(a) as being unpatentable over Wainer *et al.* in view of Wang *et al.* ("Mismatch-Sensitive Hybridization Detection by Peptide Nucleic Acids Immobilized on a Quartz Crystal Microbalance," *Anal. Chem.*, 69: 5200-5202 (1997)). The Examiner states that:

Wainer et al. reference [has] discussed but does not explicitly teach using quartz crystal microbalance (QCM) to detect peptide nucleic acids. Wang et al. teach using QCM biosensor to detect DNA-protein complex in a biological sample. (See abstract, page 5200, right column, second paragraph) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided Wainer et al. with the aid of QCM biosensor as taught by Wang et al. for the detection of aptamer complex, e.g. DNA-protein-metabolites, in the patient plasma sample to determine the phenotype of the patient in response to the treatment of therapeutics.

Claim 24 is dependent upon Claim 1, which has been amended. The invention of Claim 24 is not obvious over Wainer *et al.* in view of Wang *et al.* because, as established above, Wainer *et al.* do not teach or disclose a method of characterizing a metabolic phenotype of an individual to individualize a selected safe and therapeutically effective drug treatment dosing regimen for said individual. Therefore, the cited references do not reasonably suggest the claimed invention, because using a QCM biosensor, as disclosed by Wang *et al.*, in the methods taught by Wainer *et al.*, would not result in the claimed invention. In view of the foregoing, reconsideration and withdrawal of the rejection is requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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